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Claims: 1 page

Description: 11 pages

[54] Invention Title: Pharmaceutical Formulation of Mosapride Citrate

[57] Abstract:

The present invention discloses a pharmaceutical formulation for preparing mosapride citrate dispersible tablets by wet-granulating tableting method, wherein the pharmaceutical formulation comprises mosapride citrate as the active ingredient, and disintegrant, diluent, lubricant, flow aid and binder. Said pharmaceutical formulation is suitable for the preparation of dispersible tablets that can be fully disintegrated in the water at 19°C -21°C within 3 minutes and pass the sieve No. 2, and the dissolution rate of dispersible tablets also meets the relevant criterions.

**What is claimed is:**

**1. A pharmaceutical formulation suitable for preparing dispersible tablets by wet-granulating tableting method, comprising 3% by weight of mosapride citrate based on the total weight of the formulation, and appropriate excipients and accessories.**

**2. The formulation according to claim 1, wherein the appropriate excipients and accessories comprise disintegrant, diluent, binder, flow aid, and lubricant.**

**3. The formulation according to claim 2, wherein the disintegrant is low substituted hydroxypropyl cellulose, sodium hydroxymethyl starch, crosslinked sodium carboxymethyl cellulose, crosslinked polyvinyl- pyrrolidone, pre-gelatinized starch, or calcium carboxymethyl cellulose.**

**4. The formulation according to claim 3, wherein the content of disintegrant is 9-30% based on the total weight of the formulation.**

**5. The formulation according to claim 2, comprising a mixture of 5-15% of starch, 14-70% of lactose, and 9-30% of microcrystalline cellulose based on the total weight of the formulation, which is used as the diluent.**

**6. The formulation according to claim 2, comprising hydroxypropylmethyl cellulose as the binder in a content of 1-2% based on the total weight of the formulation.**

**7. The formulation according to claim 2, comprising micropowdered silica gel as the flow aid in a content of 2.5-5% based on the total weight of the formulation.**

**8. The formulation according to claim 2, comprising magnesium stearate as the lubricant in a content of 0.5-1% based on the total weight of the formulation.**

## Pharmaceutical Formulation of Mosapride Citrate

The present invention relates to a dosage form of digestive tract dynamic drug, to be specific, mosapride citrate dispersible tablets.

Mosapride citrate, i.e. ( $\pm$ )-4-amino-5-chloro-2-ethoxy-N-{{[4-(4-fluorobenzyl)-2-morpholinyl]methyl} benzamide citrate dihydrate, and is a third generation gastric dynamic drug developed by Dainippon Seiyaku KK, which can be referred to the patents, for example, JP3090274, EP0243959, and US4870074. Mosapride citrate is a novel gastric dynamic drug, a potent selective 5-HT<sub>4</sub> receptor agonist, which increases the acetylcholine release of nerve end and thereby to promote gastric emptying [katayama K, Morio Y, Haga K, et al., cisapride, a gastroprokinetic agent, binds to 5-HT<sub>4</sub> receptors [J]. *Nippon Yakurigaku Zasshi*, 1995, 105(6):461-468]. Mosapride citrate is clinically used for the treatment of chronic gastritis, functional dyspepsia, reflux esophagitis, and gastrointestinal track symptoms associated with operations [Jinhua, Zhangtiejun, Mosapride citrate, a novel gastric dynamic drug, *Yaoxue Jinzhan*, 2000, 24(5): 306-308].

At present, dosage forms of mosapride citrate include 2.5mg, 5mg tablets, and 10mg/bag powder. The limitations and drawbacks of using the powder are as follows: (1) inconvenient in use; and (2) difficult in preservation, i.e., easy to deteriorate and to be contaminated.

On the other hand, normal mosapride citrate tablets also have the following drawbacks: (1) normal mosapride citrate tablets have a slow dissolution rate and a small solubility, which influence their absorption; and (2) normal mosapride citrate tablets are large in volume or are taken with multiple tablets each time, which bring about many troubles especially to the old or the children or patients with dysphagia of solid things.

Thus, it is desirably to have new mosapride citrate dosage forms with merits of easy administration, rapid release, quick absorption and high bioavailability are needed for overcoming the above drawbacks. The object of the present invention is to provide formulations for such new dosage forms and a process for the preparation thereof, i.e., formulations of mosapride citrate dispersible tablets and a process for the preparation thereof.

To achieve the above object, the following technical solutions are employed in the present invention.

To prepare an appropriate composition of mosapride citrate dispersible tablets, it is necessary to study the incompatibility of the physical/chemical properties of the active

ingredients, moreover, suitable excipients are to be screened according to different requirements. Since the excipients and accessories of the composition depend significantly on the process for preparing the dispersible tablets, a wet-granulating tableting process is employed to prepare the dispersible tablets.

According to Pharmacopoeia of People's Republic of China Edition 2000, the parameters of dispersible tablets are defined as follows.

**Dispersion uniformity:** Placing 2 dispersible tablets in 100ml of water and shaking, and the tablets shall disintegrate completely and pass through sieve No. 2 in  $20^{\circ}\text{C}\pm 1^{\circ}\text{C}$  water within 3 minutes.

**Solubility test:** measuring according to the method for detecting dissolution rate (Pharmacopoeia of People's Republic of China Edition 2000, Part II, Annex XC, the third method).

The present invention provides a formulation for preparing dispersible tablets which include mosapride citrate used as the active ingredient, disintegrant, diluent, lubricant, flow aid and binder.

The active ingredient in the formulation of the present invention is mosapride citrate which has an amount of 3% based on the total weight of the formulation. Mosapride citrate can be prepared based on the methods disclosed in the patents such as JP3090274, EP0243959, US4870074.

Since the key parameter of dispersible tablets is the disintegration rate in water, appropriate selection of the disintegrant is one of the most important steps. In the formulation of the present invention, the disintegrant such as, low substituted hydroxypropyl cellulose (Ls-HPC), sodium hydroxymethyl starch (CMS-Na), crosslinked sodium carboxymethyl cellulose (CCMC-Na), crosslinked polyvinylpyrrolidone (PVPP), pregelatinized starch, calcium carboxymethyl cellulose. The content of disintegrant is 9-30% based on the total weight of the formulation.

In the formulation of the present invention, the suitable diluent is a mixture comprising 5-15.5% by weight of starch, 14-70% by weight of lactose, and 9-30% by weight of microcrystalline cellulose relative to the total weight of the formulation, wherein the microcrystalline cellulose also acts as a disintegrant.

In the formulation of the present invention, hydroxypropylmethyl cellulose (HPMC) is used as the binder, and has a content of 1-2% based on the total weight of the formulation.

In the formulation of the present invention, magnesium stearate is used as the lubricant, and has a content of 0.5-1% based on the total weight of the formulation.

In the formulation of the present invention, micropowdered silica gel is used as the flow aid, and has a content of 2.5-5% based on the total weight of the formulation.

The present invention is further demonstrated by the following examples.

#### Example 1

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	10%
Lactose	51%
Microcrystalline cellulose	11%
Low substituted hydroxypropyl cellulose	20%
Hydroxypropylmethyl cellulose	1%
Magnesium stearate	0.7%
Micropowdered Silica gel	3.3%

Preparation process: passing the active ingredient mosapride citrate through a 180 mesh sieve, and passing all the accessories through a 120 mesh sieve, for the following steps:

(1) Weighing starch, lactose, microcrystalline cellulose and disintegrant according to the amounts in the formulation, and mixing them uniformly in a suitable mixer;

(2) Weighing mosapride citrate according to the above amount in the formulation, adding into the mixture of accessories for dilution by an equal-quantity successive increase method, sufficiently mixing and passing through 40 mesh sieve each time until the total stuff is mixed uniformly;

(3) Preparing a soft mass by using a solution of 2% HPMC in 40% ethanol, preparing wet granules with a 18 mesh sieve;

(4) Drying the wet granules of step (3) at 50°C by ventilation, taking out after 2 hours, and trimming granules through a 18 mesh sieve;

(5) Weighing micro-powdered silica gel and magnesium stearate according to the amounts in the formulation, mixing them uniformly with the granules of step (4); and

(6) Tableting by using a tablet machine with 8mm dies.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 2

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	13%
Lactose	40%
Microcrystalline cellulose	23%
Low substituted hydroxypropyl cellulose	15%
Hydroxypropylmethyl cellulose	1.5%
Magnesium stearate	0.5%
Mcropowered Silica gel	4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 3

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	10%
Lactose	48%
Microcrystalline cellulose	17%
Low substituted hydroxypropyl cellulose	17%
Hydroxypropylmethyl cellulose	1.3%
Magnesium stearate	0.7%
Micropowed silica gel	3%

The preparation process is identical to that of Example 1.

Example 3 is the optimal example of the present invention.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that

meets the criterion.

#### Example 4

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	8%
Lactose	44%
Microcrystalline cellulose	15%
Sodium hydroxymethyl starch	24%
Hydroxypropylmethyl cellulose	1.7%
Magnesium stearate	0.8%
Micropoweed Silica gel	3.5%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 5

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	15%
Lactose	20%
Microcrystalline cellulose	27%
Sodium hydroxymethyl starch	28%
Hydroxypropylmethyl cellulose	1.8%
Magnesium stearate	0.7%
Micropowdered silica gel	4.5%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 6

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	9%
Lactose	62%
Microcrystalline cellulose	10%
Sodium hydroxymethyl starch	10%
Hydroxypropylmethyl cellulose	1.9%
Magnesium stearate	0.7%
Micropowdered silica gel	3.4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 7

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	11%
Lactose	35%
Microcrystalline cellulose	20%
Sodium crosslinked carboxymethylcellulose	25%
Hydroxypropylmethyl cellulose	1.4%
Magnesium stearate	0.6%
Micropowdered silica gel	4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 8

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%



Starch	10%
Lactose	51%
Microcrystalline cellulose	11%
Sodium crosslinked carboxymethylcellulose	20%
Hydroxypropylmethyl cellulose	1%
Magnesium stearate	0.7%
Micropowdered silica gel	3.3%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 9

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	13%
Lactose	40%
Microcrystalline cellulose	23%
Sodium crosslinked carboxymethylcellulose	15%
Hydroxypropylmethyl cellulose	1.5%
Magnesium stearate	0.5%
Micropowdered silica gel	4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 10

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	10%
Lactose	48%
Microcrystalline cellulose	17%
Crosslinked polyvinylpyrrolidone	17%

Hydroxypropylmethyl cellulose	1.3%
Magnesium stearate	0.7%
Micropowdered silica gel	3%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 11

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	8%
Lactose	44%
Microcrystalline cellulose	15%
Crosslinked polyvinylpyrrolidone	24%
Hydroxypropylmethyl cellulose	1.7%
Magnesium stearate	0.8%
Micropowdered silica gel	3.5%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 12

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	15%
Lactose	20%
Microcrystalline cellulose	27%
Crosslinked polyvinylpyrrolidone	28%
Hydroxypropylmethyl cellulose	1.8%
Magnesium stearate	0.7%
Micropowdered silica gel	4.5%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 13

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	9%
Lactose	62%
Microcrystalline cellulose	10%
Pre-gelatinized starch	10%
Hydroxypropylmethyl cellulose	1.9%
Magnesium stearate	0.7%
Micropowdered silica gel	3.4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 14

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	11%
Lactose	35%
Microcrystalline cellulose	20%
Pre-gelatinized starch	25%
Hydroxypropylmethyl cellulose	1.4%
Magnesium stearate	0.6%
Micropowdered silica gel	4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 15

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	10%
Lactose	51%
Microcrystalline cellulose	11%
Pre-gelatinized starch	20%
Hydroxypropylmethyl cellulose	1%
Magnesium stearate	0.7%
Micropowdered silica gel	3.3%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 16

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	10%
Lactose	51%
Microcrystalline cellulose	11%
Calcium carboxymethyl cellulose	20%
Hydroxypropylmethyl cellulose	1%
Magnesium stearate	0.7%
Micropowdered silica gel	3.3%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 17

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%

Starch	13%
Lactose	40%
Microcrystalline cellulose	23%
Calcium carboxymethyl cellulose	15%
Hydroxypropylmethyl cellulose	1.5%
Magnesium stearate	0.5%
Micropowdered silica gel	4%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

#### Example 18

Dispersible tablets are prepared according to the following pharmaceutical formulation.

Components	% (by weight)
Mosapride citrate	3%
Starch	10%
Lactose	48%
Microcrystalline cellulose	17%
Calcium carboxymethyl cellulose	17%
Hydroxypropylmethyl cellulose	1.3%
Magnesium stearate	0.7%
Micropowdered silica gel	3%

The preparation process is identical to that of Example 1.

The obtained dispersible tablets have the following features: fully disintegrating and passing through No. 2 sieve within 3 minutes in 19°C -21°C water, and having a dissolution rate that meets the criterion.

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权利要求书 1 页 说明书 11 页 附图页数 0 页

[54] 发明名称 枸橼酸莫沙必利的制药用配方

[57] 摘要

本发明公开了一种适合于用湿法制粒压片法制备分散片的枸橼酸莫沙必利的制药用配方,其中除含有活性成分枸橼酸莫沙必利外,还含有崩解剂、稀释剂、润滑剂、助流剂、粘合剂。所述药用配方适用于制备可分散片剂,该分散片在 19℃ - 21℃ 水中,3 分钟全部崩解并通过 2 号筛。溶出度也符合有关规定。

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## 权 利 要 求 书

1、以含量在总配方重量的 3% 的枸橼酸莫沙必利作为活性成分，加有合适的赋形剂和辅助剂，适合用湿法制粒压片法制备分散片剂的制药用配方。

2、如权利要求 1 所述的配方，其中所述的合适的赋形剂和辅助剂包括崩解剂、稀释剂、粘合剂、助流剂、润滑剂。

3、如权利要求 2 所述的配方，其中崩解剂是低取代羟丙基纤维素、羟甲淀粉钠、交联羧甲纤维素钠、交联聚乙烯吡咯烷酮、预胶化淀粉、羧甲基纤维素钙。

4、如权利要求 3 所述的配方，崩解剂的含量为总配方重量的 9-30%。

5、如权利要求 2 所述的配方，含有总配方重量的 5-15% 的淀粉和总配方重量的 14-70% 的乳糖和总配方重量的 9-30% 微晶纤维素三者的混合物作为稀释剂。

6、如权利要求 2 所述的配方，含有羟丙甲纤维素作为粘合剂，其含量为总配方重量的 1-2%。

7、如权利要求 2 所述的配方，含有微粉硅胶作为助流剂，其含量为总配方重量的 2.5-5%。

8、如权利要求 2 所述的配方，含有硬脂酸镁作为润滑剂，其含量为总配方重量的 0.5-1%。

# 说明书

## 枸橼酸莫沙必利的制药用配方

本发明涉及一种消化道动力药的剂型，具体讲是枸橼酸莫沙必利分散片。

枸橼酸莫沙必利，即(±)—4—氨基—5—氯—2—乙氧基—N—{[4—(4—氟苄基)—2—吗啉]甲基}苯甲酰胺枸橼酸盐二水合物，为大日本制药株式会社开发的第三代胃动力药，参见例如日本专利 JP3090274，欧洲专利 EP0243959，美国专利 US4870074。枸橼酸莫沙必利为新型胃动力药，强效选择性 5—HT<sub>4</sub> 受体激动剂，使神经末梢的乙酰胆碱释放增加，从而促进胃排空 [Katayama K, Morio Y, Haga K, et al. cisapride. a gastroprokinetic agent, binds to 5—HT<sub>4</sub> receptors [J]. Nippon Yakurigaku Zasshi, 1995, 105 (6): 461—468.] 临床用于慢性胃炎，功能性消化不良，反流性食管炎及手术伴随的一系列胃肠道症状的缓解。[金华、张铁军，枸橼酸莫沙必利——新型胃动力药，药学进展，2000，24 (5)：306—308]。

现枸橼酸莫沙必利的剂型有 2.5mg、5mg 片剂和 10mg/袋散剂。使用散剂有如下一些限制和不足之处：

- 1、使用不便。
- 2、不易保存，易变质和污染。

另一方面，枸橼酸莫沙必利的普通片剂也存在以下缺点：

- 1、普通片剂存在溶解速度慢，溶解度小的缺点，对药物的吸收有一定的影响。
- 2、普通片剂的体积较大，或一次常用多片，特别是给老、幼和吞服固体存在困难的病人治疗带来了麻烦。

因而需要枸橼酸莫沙必利新的给药剂型来克服以上缺点，所述新剂型可方便病人用药，并可使药物溶出迅速，吸收快，生物利用度高。本发明的目的是提供这种新剂型的配方及其制备方法，也就是提供枸橼酸莫沙必利分散片的配方及其制备方法。

为实现上述目的，本发明采用以下技术方案：

制备用于生产可分散片剂的适当的组合物不但需要研究活性成分的理化性质的配伍禁忌，还要寻找符合不同要求的合适的赋形剂。由于组合物的赋形剂和辅料，很大程度上取决于制备该分散片剂所选择的方法。湿法制粒压片是制备该分散片剂所选择的方法。



根据中国药典 2000 版，定义分散片的参数如下：

分散均匀性 取分散片 2 片，置 100ml 水中振摇，在  $20^{\circ}\text{C} \pm 1^{\circ}\text{C}$  水中，3 分钟应全部崩解并通过 2 号筛。

溶出度检查 溶出度测定方法（中国药典 2000 年版二部附录 XC 第三法）测定。

由本发明提供的适合制备分散片的配方，除了由活性成分枸橼酸莫沙必利外，还含有崩解剂、稀释剂、润滑剂、助流剂、粘合剂。

枸橼酸莫沙必利是本发明配方中的活性成分。在配方中枸橼酸莫沙必利的含量占总配方重量的 3%。枸橼酸莫沙必利可按例如日本专利 JP3090274，欧洲专利 EP0243959，美国专利 US4870074 中所述方法制备。

因为分散片的关键参数是它们在水中的崩解速度，所以选择合适的崩解剂是最重要的步骤之一。本发明配方中的崩解剂有低取代羟丙基纤维素

（Ls—HPC）、羟甲淀粉钠（CMS—Na）、交联羧甲纤维素钠（CCMC—Na）、交联聚乙烯吡咯烷酮（PVPP）、预胶化淀粉、羧甲基纤维素钙。崩解剂的含量为总配方重量的 9-30%。

作为本发明配方的合适稀释剂为：含有总配方重量的 5-15.5% 的淀粉和总配方重量的 14-70% 的乳糖和总配方重量的 9-30% 微晶纤维素三者的混合物。其中微晶纤维素兼有崩解剂作用。

作为本发明配方的粘合剂为羟丙甲纤维素（HPMC），其含量为总配方重量的 1-2%。

作为本发明配方的润滑剂为硬脂酸镁，其含量为总配方重量的 0.5-1%。

作为本发明配方的助流剂为微粉硅胶，其含量为总配方重量的 2.5-5%。

下面实施例用来说明本发明的具体实施。

#### 实施例 1

分散片由以下制药用配方制备：

成分	%（按重量计算）
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	51%
微晶纤维素	11%
低取代羟丙基纤维素	20%
羟丙甲纤维素	1%

硬脂酸镁	0.7%
微粉硅胶	3.3%

#### 制备方法

活性成分枸橼酸莫沙必利过 180 目筛，所有辅料过 120 目筛备用。

1. 称取配方量的淀粉、乳糖、微晶纤维素和崩解剂，用适宜的混合器混合均匀。
2. 称取以上配方量的枸橼酸莫沙必利，将其以等量递加稀释法加入混合辅料中，每次充分混合过 40 目筛直至完全混合均匀。
3. 用 2%HPMC40%乙醇液制备软材，18 目筛制湿颗粒。
4. 将上项所得湿颗粒于 50℃通风干燥，2 小时取出后 18 目筛整粒。
5. 称取以上配方量微粉硅胶及硬脂酸镁混合上项颗粒，充分混匀。
6. 于压片机上用 8mm 冲压制，即得。

得到的分散片具下列特性：

在 19℃～21℃水中，3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 2

分散片由以下制药用配方制备：

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	13%
乳糖	40%
微晶纤维素	23%
低取代羟丙基纤维素	15%
羟丙甲纤维素	1.5%
硬脂酸镁	0.5%
微粉硅胶	4%

制备方法同实施例 1

得到的分散片具下列特性：

在 19℃～21℃水中，3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 3

分散片由以下制药用配方制备：

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	48%
微晶纤维素	17%
低取代羟丙基纤维素	17%
羟丙甲纤维素	1.3%
硬脂酸镁	0.7%
微粉硅胶	3%

制备方法同实施例 1

本实施例为本发明的最佳实施例。

得到的分散片具下列特性：

在 19℃ ~ 21℃ 水中，3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 4

分散片由以下制药用配方制备：

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	8%
乳糖	44%
微晶纤维素	15%
羟甲淀粉钠	24%
羟丙甲纤维素	1.7%
硬脂酸镁	0.8%
微粉硅胶	3.5%

制备方法同实施例 1

得到的分散片具下列特性：

在 19℃ ~ 21℃ 水中，3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 5

分散片由以下制药用配方制备：

成分	% (按重量计算)
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枸橼酸莫沙必利	3%
淀粉	15%
乳糖	20%
微晶纤维素	27%
羟甲淀粉钠	28%
羟丙甲纤维素	1.8%
硬脂酸镁	0.7%
微粉硅胶	4.5%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 6

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	9%
乳糖	62%
微晶纤维素	10%
羟甲淀粉钠	10%
羟丙甲纤维素	1.9%
硬脂酸镁	0.7%
微粉硅胶	3.4%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 7

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	11%

乳糖	35%
微晶纤维素	20%
交联羧甲纤维素钠	25%
羟丙甲纤维素	1.4%
硬脂酸镁	0.6%
微粉硅胶	4%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

实施例 8

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	51%
微晶纤维素	11%
交联羧甲纤维素钠	20%
羟丙甲纤维素	1%
硬脂酸镁	0.7%
微粉硅胶	3.3%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

实施例 9

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	13%
乳糖	40%
微晶纤维素	23%

交联羧甲纤维素钠	15%
羟丙甲纤维素	1.5%
硬脂酸镁	0.5%
微粉硅胶	4%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

实施例 10

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	48%
微晶纤维素	17%
交联聚乙烯吡咯烷酮	17%
羟丙甲纤维素	1.3%
硬脂酸镁	0.7%
微粉硅胶	3%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

实施例 11

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	8%
乳糖	44%
微晶纤维素	15%
交联聚乙烯吡咯烷酮	24%
羟丙甲纤维素	1.7%

硬脂酸镁 0.8%

微粉硅胶 3.5%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 12

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	15%
乳糖	20%
微晶纤维素	27%
交联聚乙烯吡咯烷酮	28%
羟丙甲纤维素	1.8%
硬脂酸镁	0.7%
微粉硅胶	4.5%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 13

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	9%
乳糖	62%
微晶纤维素	10%
预胶化淀粉	10%
羟丙甲纤维素	1.9%
硬脂酸镁	0.7%
微粉硅胶	3.4%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

实施例 14

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	11%
乳糖	35%
微晶纤维素	20%
预胶化淀粉	25%
羟丙甲纤维素	1.4%
硬脂酸镁	0.6%
微粉硅胶	4%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

实施例 15

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	51%
微晶纤维素	11%
预胶化淀粉	20%
羟丙甲纤维素	1%
硬脂酸镁	0.7%
微粉硅胶	3.3%

制备方法同实施例 1

得到的分散片具下列特性:



在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 16

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	51%
微晶纤维素	11%
羧甲基纤维素钙	20%
羟丙甲纤维素	1%
硬脂酸镁	0.7%
微粉硅胶	3.3%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

#### 实施例 17

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	13%
乳糖	40%
微晶纤维素	23%
羧甲基纤维素钙	15%
羟丙甲纤维素	1.5%
硬脂酸镁	0.5%
微粉硅胶	4%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定

**实施例 18**

分散片由以下制药用配方制备:

成分	% (按重量计算)
枸橼酸莫沙必利	3%
淀粉	10%
乳糖	48%
微晶纤维素	17%
羧甲基纤维素钙	17%
羟丙甲纤维素	1.3%
硬脂酸镁	0.7%
微粉硅胶	3%

制备方法同实施例 1

得到的分散片具下列特性:

在 19℃ ~ 21℃ 水中, 3 分钟全部崩解并通过 2 号筛。

溶出度 符合规定